Analisis jalur apoptosis ko-kemoterapi nanokurkumin-cisplatin di hepar pada model kanker ovarium tikus: tinjauan khusus pada bax dan kaspase-3 = Analysis of the nanocurcumin-cisplatin co-chemotherapy apoptosis pathway in the liver of mouse ovarian cancer models: overview on bax and caspase-3

Natasha Talya, author

Abstrak

Latar Belakang: Cisplatin telah menjadi terapi lini pertama untuk kanker ovarium, namun efek samping terbesar cisplatin adalah peningkatan resistensi sel kanker yang menyebabkan hepatotoksisitas pada sel normal. Kurkumin terbukti memiliki sifat hepatoprotektif, tetapi efek terapeutik kurkumin terbatas karena memiliki bioavailabilitas yang rendah. Penggunaan kitosan nanopartikel pada kurkumin telah terbukti meningkatkan bioavailabilitas kurkumin sehingga efektivitasnya lebih besar. Penelitian ini dilaksanakan untuk melihat pengaruh nanokurkumin terhadap hepatotoksisitas akibat pemberian cisplatin. Tujuan: Membandingkan pengaruh kurkumin dan nanopartikel kurkumin untuk digunakan sebagai ko-kemoterapi dengan cisplatin pada kanker ovarium tikus yang ditinjau melalui jalur apoptosis, khususnya marker Bax dan Kaspase-3. Metode: Penelitian ini merupakan penelitian eksperimental in vivo pada model kanker ovarium tikus betina galur Wistar yang diinduksi 7,12-dimethybenzen[a]anthracene (DMBA) dan dilaksanakan di Departemen Farmakologi dan Terapeutik Fakultas Kedokteran Universitas Indonesia sejak bulan Juni 2019 hingga Juni 2020. Cisplatin diberikan dalam dosis sebesar 4 mg/kgBB secara intraperitoneal. Kurkumin dan nanokurkumin diberikan dalam dosis oral sebesar 100 mg/kgBB. Organ tersimpan hepar yang diambil dari 25 ekor tikus terbagi menjadi 5 kelompok perlakuan, yaitu kelompok tikus normal, model kanker ovarium tikus, terapi cisplatin, terapi cisplatin + kurkumin, dan terapi cisplatin + nanokurkumin. Setelah dikelompokkan, dilakukan homogenisasi sampel yang terpilih. Lalu, RNA Bax dan Kaspase-3 diisolasi dari homogenat sampel organ hepar dan cDNA kedua gen disintesis. Kemudian, tingkat ekspresi mRNA Bax dan Kaspase-3 pada hepar diukur menggunakan qRT-PCR. Data ekspresi mRNA Bax dan Kaspase-3 dianalisis dan diuji korelasi antarkelompok menggunakan aplikasi SPSS. Hasil: Tidak ada perbedaan yang signifikan antara kelima kelompok pada tingkat ekspresi mRNA Bax (p=0,372) dan Kaspase-3 (p=0,111). Kesimpulan: Tidak ditemukan pengaruh kurkumin dan nanokurkumin terhadap ekspresi mRNA Bax dan Kaspase-3 organ hepar pada model kanker ovarium tikus setelah pemberian terapi cisplatin. <hr /> Background: Cisplatin has become the first-line therapy for ovarian cancer, but it has a side effect of increasing cancer cell resistance which causes hepatotoxicity in normal cells. Curcumin has been shown to have hepatoprotective properties, but its therapeutic effect is limited because of its low bioavailability. The use of chitosan nanoparticles in curcumin has been shown to increase the bioavailability of curcumin. This research was conducted to see the effect of nanocurcumin on hepatotoxicity due to cisplatin administration. Aim: Comparing the effect of curcumin and curcumin nanoparticles as co-chemotherapy with cisplatin in rat ovarian cancer that is evaluated through apoptotic pathways, specifically Bax and Kaspase-3 markers. Methods: This research is an in vivo experimental study on a female ovarian

cancer model of Wistar rats induced 7,12-dimethybenzen[a]anthracene (DMBA) and was carried out in the Department of Pharmacology and Therapeutics of the Faculty of Medicine, University of Indonesia from June 2019 to June 2020. Cisplatin is given in doses of 4 mg/kgBW intraperitoneal. Curcumin and nanocurcumin are given in oral doses of 100 mg/kgBW. Stored liver organs which was taken from 25 rats was divided into 5 treatment groups which are normal, ovarian cancer model, cisplatin therapy, cisplatin + curcumin therapy, and cisplatin + nanocurcumin therapy group. After the samples are grouped, homogenization of the selected sample is carried out. Then, the Bax and Kaspase-3 RNA were isolated from the homogenate samples and the cDNA of the two genes was synthesized. Then, the levels of Bax and Kaspase-3 mRNA expressions in the liver were measured using qRT-PCR. Bax and Kaspase-3 mRNA expressions were analyzed and tested intergroup correlations using the SPSS application. Results: There were no significant differences between the five groups in the expression levels of Bax mRNA (p=0,372) and Kaspase-3 (p=0,111). Conclusion: This study shows no effect of curcumin and nanocurcumin on the expression of Bax and Caspase-3 liver organ mRNA in rat ovarian cancer models after cisplatin therapy.</p>